CLAIMS

What is claimed is:

1. A method for producing spray-dried particles having improved stability of a bioactive agent comprising:

(a) combining a bioactive agent, a phospholipid and a co-solvent, said co-solvent including an aqueous solvent and an organic solvent, to form a mixture; and

(b) spray-drying said mixture to produce spray-dried particles having improved stability of the bioactive agent.

2. The method of Claim 1 wherein the spray-dried particles consist essentially of the bioactive agent and the phospholipid.

3. The method of Claim 1 wherein the spray-dried particles consist of the bioactive agent and the phospholipid.

4. The method of Claim 1 wherein the phospholipid is a phospholipid endogenous to the lung.

5 The method of Claim 1 wherein the phospholipid is selected from the group consisting of phosphatidylcholines, phosphatidylethanolamines, phosphatidylglycerols, phosphatidylserines, phosphatidylinositols and combinations thereof.

6. The method of claim 1 wherein the phospholipid is present in the particles in an amount ranging from about 1 to about 99 weight %.

7. The method of Claim 1 wherein the bioactive agent includes a protein.

8. The method of claim 7 wherein the protein is human growth hormone.

9. The method of Claim 7 wherein the protein is present in the spray-dried particles in an amount ranging from about 1 to about 99 weight %.

10. The method of Claim 7 wherein protein stability is measured by SEC-HPLC.

11. The method of Claim 7 wherein the spray-dried particles retain at least about 70% protein integrity when stored at about 25°C and about 60% relative humidity conditions for six weeks.

12. The method of Claim 7 wherein the spray-dried particles retain at least about 50% protein integrity when stored at about 40°C and about 75% relative humidity conditions for six weeks.

13. The method of Claim 1 wherein the bioactive agent includes a peptide.

14. The method of Claim 1 wherein the bioactive agent includes a biologically active macromolecule other than a protein or peptide.

15. The method of Claim 1 wherein the bioactive agent is a therapeutic, prophylactic or diagnostic agent.

16. The method of Claim 1 wherein the combined bioactive agent and phospholipid concentration in said mixture is at least 0.1 weight/volume %.

17. The method of Claim 1 wherein the co-solvent includes an alcohol.

18. The method of Claim 1 wherein the organic solvent is present in the co-solvent

in a concentration of at least 50 volume %.

19. The method of Claim 1 wherein the spray-dried particles have a tap density less than about 0.4 g/cm^3.

20. The method of Claim 19 wherein the spray-dried particles have a tap density less than about 0.1 g/cm^3.

21. The method of Claim 19 wherein the spray-dried particles have a tap density less than about 0.05 g/cm^3.

22. The method of Claim 19 wherein the spray-dried particles have a median geometric diameter of between about 5 microns and about 30 microns.

23. The method of Claim 19 wherein the spray-dried particles have an aerodynamic diameter of between about 1 micron and about 5 micron.

24. The particles produced by the method of Claim 1.

25. A method comprising administering to the respiratory tract of a patient in need of treatment, prophylaxis or diagnosis an effective amount of the spray-dried particles produced by the method of Claim 1.

26. A method for producing spray-dried particles having improved stability of a bioactive agent comprising:

(a) combining a bioactive agent, a phospholipid and an organic solvent, to form a mixture; and

(b) spray-drying said mixture to produce spray-dried particles having improved stability of the bioactive agent.

27. The method of Claim 26 wherein the spray-dried particles consist essentially of the bioactive agent and the phospholipid.

28. The method of Claim 26 wherein the spray-dried particles consist of the bioactive agent and the phospholipid.

29. The method of Claim 26 wherein the phospholipid is a phospholipid endogenous to the lung.

30 The method of Claim 26 wherein the phospholipid is selected from the group consisting of phosphatidylcholines, phosphatidylethanolamines, phosphatidylglycerols, phosphatidylserines, phosphatidylinositols and combinations thereof.

31. The method of claim 26 wherein the phospholipid is present in the particles in an amount ranging from about 1 to about 99 weight %.

32. The method of Claim 26 wherein the bioactive agent includes a protein.

33. The method of claim 32 wherein the protein is human growth hormone.

34. The method of Claim 32 wherein the protein is present in the spray-dried particles in an amount ranging from about 1 to about 99 weight %.

35. The method of Claim 32 wherein protein stability is measured by SEC-HPLC..

36. The method of Claim 32 wherein the spray-dried particles retain at least about 70% protein integrity when stored at about 25°C and about 60% relative humidity conditions for six weeks.

37. The method of Claim 32 wherein the spray-dried particles retain at least about 50% protein integrity when stored at about 40°C and about 75% relative humidity conditions for six weeks.

38. The method of Claim 26 wherein the bioactive agent includes a peptide.

39. The method of Claim 26 wherein the bioactive agent includes a biologically active macromolecule other than a peptide or a protein.

40. The method of Claim 26 wherein the bioactive agent is a therapeutic, prophylactic or diagnostic agent.

41. The method of Claim 26 wherein the combined bioactive agent and phospholipid concentration in said mixture is at least 1 weight/volume %.

42. The method of Claim 26 wherein the solvent includes an alcohol.

43. The method of Claim 26 wherein the spray-dried particles have a tap density less than about 0.4 g/cm^3.

44. The method of Claim 43 wherein the spray-dried particles have a tap density less than about 0.1 g/cm^3.

45. The method of Claim 43 wherein the spray-dried particles have a tap density less than about 0.05 g/cm^3.

46. The method of Claim 43 wherein the spray-dried particles have a median geometric diameter of between about 5 microns and about 30 microns.

47. The method of Claim 43 wherein the spray-dried particles have an aerodynamic diameter of between about 1 micron and about 5 micron.

48. The particles produced by the method of Claim 26

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49. A method comprising administering to the respiratory tract of a patient in need of treatment, prophylaxis or diagnosis an effective amount of the spray-dried particles produced by the method of Claim 26.

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